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The Effect of Hydrogen Bonding on the Rates of Inversion of 1-Hydroxy-5, 7-dihydrodibenz[*c*, *e*]oxepin

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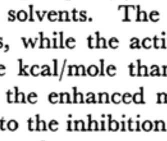
The rates of inversion of 1-hydroxy-5, 7-dihydrodibenz[*c*, *e*]oxepin (I) and its methyl ether (II) have been measured by NMR line-shape method in several solvents. The activation parameters for inversion of II are insensitive to the change in solvents, while the activation energy of I in strongly proton-accepting DMSO is clearly smaller by one kcal/mole than that of I in $CDCl_3$ and those of II. The solvent effect may be due partly to the enhanced mesomerism of the biphenyl system as the result of hydrogen bonding and partly to the inhibition of the intramolecular O–H$\cdots\pi$ interaction which will otherwise stabilize the non-planar ground state in the inert solvents.

NMR spectroscopy has lately been applied to the study of rates of the restricted rotation of biphenyls with the rate constants of 1 to 10^3 sec^{-1} by observing the temperature-dependent signal shape of the dissymmetrically disposed methylene protons which are originally diastereomeric but tend to be equalized by mutual exchange of their magnetic environments through rotation around the pivot bond of the biphenyl skeleton.[1-5] Before the advent of this NMR technique of kinetics, rates of the restricted rotation and inversion of biphenyl derivatives had solely been measured by following rates of racemization of the optically active biphenyls through polarimetry.[6,7] Although some criticisms have been thrown on both theoretical and practical conformities of the kinetic parameters obtained by the two independent methods,[8,9] the equivalence between them has been demonstrated experimentally by comparing directly the kinetic results derived from the two methods with the same rate process.[5,10] It has also been demonstrated that the solvent effect on the rates of biphenyl inversion is rather small as far as there is no special solute-solvent interaction.[4,5,11] In the present paper the NMR method is developed to explore the effect of solvents on the rates of inversion of 1-hydroxy-5, 7-dihydrodibenz[*c*, *e*]oxepin (I) and its methyl ether (II), where strong solute-solvent interaction may be expected to take place in the former through hydrogen bonding when a suitable solvent is used.



I (R=H)

II (R=CH_3)

Experimental

Materials and Solvents. *1-Hydroxy-5, 7-dihydrodibenz[c, e]oxepin (I).* Preparation of this compound was described elswhere.[12]

1-Methoxy-5, 7-dihydrodibenz[c, e]oxepin (II). I was methylated with dimethyl sulfate as usual to give an oil, bp 153°C/2 mmHg. Found: C, 79.44; H, 6.33%. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24%.

All the solvents were of spectro-grade containing enough TMS to make the reference signals of comparable intensity to those of CH_2 resonances investigated. To dimethyl-d_6 sulfoxide was added 5% w/w acetone-d_6 in order to lower the freezing point.

Spectral Measurements. The NMR spectra were obtained on a Varian A-60 spectrometer operating at 60 Mc/sec and equipped with a variable temperature accessory. TMS was used as the internal reference,

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1) W. L. Meyer and R. B. Meyer, *J. Am. Chem. Soc.*, **85**, 2170 (1963).

2) M. Ōki, H. Iwamura and N. Hayakawa, This Bulletin, **36**, 1542 (1963); **37**, 1865 (1964).

3) R. J. Kurland, M. B. Rubin and W. B. Wise, *J. Chem. Phys.*, **40**, 2426 (1964).

4) I. O. Sutherland and M. V. J. Ramsay, *Tetrahedron*, **21**, 3401 (1965).

5) M. Ōki and H. Iwamura, *ibid.*, **24**, 2377 (1968).

6) R. Kuhn and O. Albrecht, *Liebigs Ann.*, **455**, 272 (1927).

7) D. M. Hall and M. M. Harris, *J Chem. Soc.*, **1960**, 490.

8) H. S. Gutowsky, *J. Chem. Phys.*, **25**, 1228 (1956).

9) D. M. Hall and T. M Poole, *J. Chem. Soc.*, **1966**, 1034.

10) While the preparation of this paper, the authors became aware of a report confirming the soundness of the kinetic measurements by NMR line shapes by comparing with the rate of equilibration of isomeric *N*-benzyl-*N*, 2, 4, 6-tetramethylbenzamides (A. Mannschreck, A. Mattheus and G. Rissmann, *J. Mol. Spectry.*, **23**, 15 (1967)).

11) B. M. Graybill and J. E. Leffler, *J. Phys. Chem.*, **63**, 1461 (1959).

12) M. Ōki and H. Iwamura, *J. Am. Chem. Soc.*, **89**, 576 (1967).

and the calibration of the spectrometer checked by the usual side-band technique. Temperature reading was calibrated by examining the CH_3 and OH signal separation of a methanol sample as prescribed in the instruction manuals, and the reading is accurate to $\pm 2.0°C$.

Within the measurement of a given sample, the strength of the radiofrequency was held sufficiently small and the spectra were assured of being far below saturation by observing no lowering in the peak intensity on a slight raising of the r.f. field. Since the apparent amplitude of the normal signals decreases as the temperature is raised mainly because of the thermal expansion of the solvent and the consequent apparent dilution, the recorder gain was adjusted to attain the desired amplitude of the signals. Each resonance was swept three times in turn without altering the controls. The usual sweep rate was 1 cps/sec.

The exchange broadening of the two interacting nuclear spin resonance signals has been written down by Alexander.[13] Under slow-exchange limit at lower temperature, the observed change in the line-width w is correlated to the life-time τ by Eq. (1);

$$\tau = \frac{1 \pm J_{AB}/\sqrt{\delta_{AB}^2 + J_{AB}^2}}{\pi(w - w_0)} \qquad (1)^{5)}$$

At the very point of the coalescence of the AB-quartet signal, τ_c is given by Eq. (2) when natural line-width in the absence of exchange, w_0, is negligible.

$$\tau_c = \frac{\sqrt{2}}{\pi\sqrt{\delta_{AB}^2 + 6J_{AB}^2}} \qquad (2)^{2,3)}$$

Above the coalescence temperature, the width of the coalesced singlet relative to that at $\tau=0$ can again be used to calculate τ from Eq. (3);

$$\tau = \frac{2(w - w_0)}{\pi\delta_{AB}^2} \qquad (3)^{4,5)}$$

Equations (1) to (3) were employed to calculate the exchange life-time from the observed change in the line shapes. The line-width in the absence of the exchange, w_0, was read directly from the CH_2 signals at enough low (−20°C) and/or high (150°C) temperature where $\tau=\infty$ and $\tau=0$ hold approximately.

Results and Discussion

In every solvent examined, both I and II at the lower temperature show double AB-quartet signals due to the presence of two pairs of the methylene groups. In Tables 1 and 2 are shown the spectral parameters. The quartet at the higher applied magnetic field can be assigned to the methylene protons attached to the benzene ring carrying the hydroxyl group and the methoxyl group in I and II, respectively. The assignment bases upon the fact that the aromatic methyl signal of *m*-methylanisole resonates at τ 7.77 which is located at the higher field than that of toluene, τ 7.66,[14] but the reverse assignment does not affect the following discussion. From the fact that the chemical shifts of the four protons on a pair of methylene groups can be differentiated, it is concluded that at these temperatures specified in Tables 1 and 2 the two benzene rings in I and II are fixed as non-planar in the sense of NMR and that the rate of restricted rotation around the pivot bond (Eq. (4)) should be less than a few times in a second.

TABLE 1. THE METHYLENE PROTON SPECTRA OF I AT THE LOWER TEMPERATURES

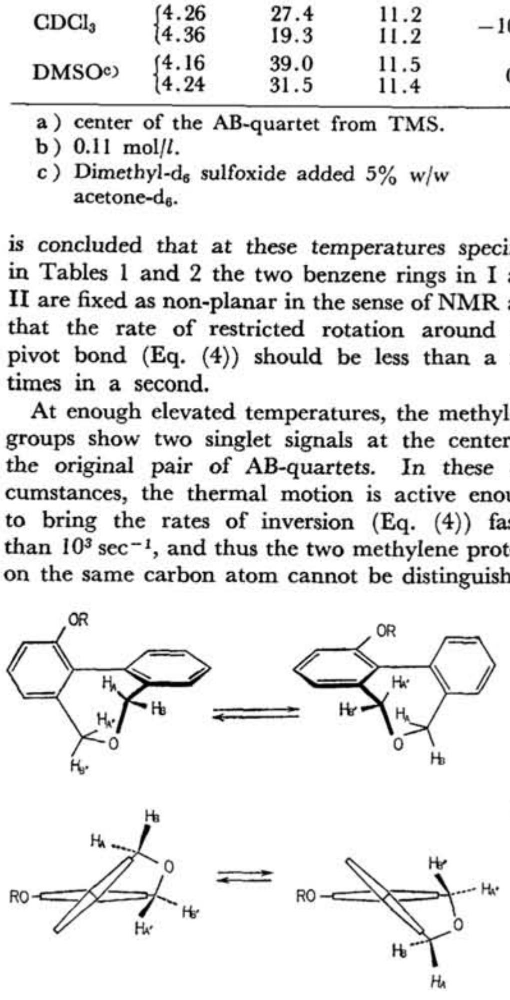
Solvent	δ ppm[a]	δ_{AB} cps	J_{AB} cps	t °C
$CDCl_3$[b]	4.31 4.41	27.4 19.1	11.2 11.0	−20
DMSO[c]	4.15 4.25	35.9 29.0	11.5 11.3	0

TABLE 2. THE METHYLENE PROTON SPECTRA OF II AT THE LOWER TEMPERATURES

Solvent	δ ppm	δ_{AB} cps	J_{AB} cps	t °C
C_2Cl_4	4.15 4.21	23.8 16.5	11.2 11.1	−20
$CDCl_3$	4.26 4.36	27.4 19.3	11.2 11.2	−10
DMSO[c]	4.16 4.24	39.0 31.5	11.5 11.4	0

a) center of the AB-quartet from TMS.
b) 0.11 mol/*l*.
c) Dimethyl-d_6 sulfoxide added 5% w/w acetone-d_6.

At enough elevated temperatures, the methylene groups show two singlet signals at the center of the original pair of AB-quartets. In these circumstances, the thermal motion is active enough to bring the rates of inversion (Eq. (4)) faster than $10^3\ sec^{-1}$, and thus the two methylene protons on the same carbon atom cannot be distinguished.



(4)

In the intermediate temperature, as the temperatures is raised, the line-width of the quartet broadens at first with the two outer lines broadening more rapidly than the two inner lines. The broadened signals coalesce gradually to a singlet, and then the peak intensity of the singlet increases at the expense of the line-width. Some typical

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[13] S. Alexander, *J. Chem. Phys.*, **37**, 967 (1962).
[14] C. Heathcock, *Canad. J. Chem.*, **40**, 1865 (1962).

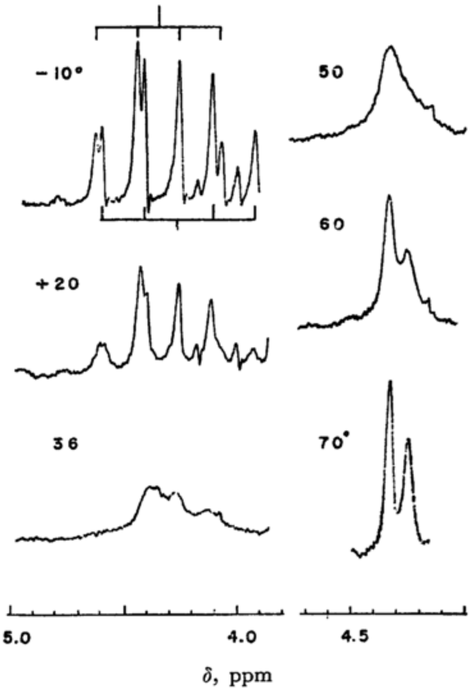

Fig. 1. NMR spectra of CH_2 protons of II in $CDCl_3$ at various temperatures.

TABLE 3. THE COALESCENCE TEMPERATURE (T_c) OF THE AB-QUARTETS AND THE LIFE-TIME (τ_c) AT THE TEMPERATURE

	Solvent	δ_{AB} cps	T_c °C	τ_c 10^{-3} sec
I	$CDCl_3$	27.4	48	11.6
		19.1	40	13.6
	DMSO	35.9	20	9.9
		29.0	10	11.2
II	C_2Cl_4	23.8	50	12.4
		16.5	40	14.2
	$CDCl_3$	27.4	46	11.6
		19.3	40	13.4
	DMSO	39.0	45	9.4
		31.5	38	10.7

experimental curves are shown in Fig. 1. Two pairs of AB-quartet overlap rather heavily on a 60 Mc/sec NMR chart, and therefore the estimated error of the coalescence temperature (T_c) is ±5°C. In Table 3 are shown the approximate T_c's of the spectra. It is to be emphasized that, in a given sample, an AB-quartet of a smaller δ_{AB} has the lower T_c. I in DMSO is unique in that it has rather low T_c's with respect to the greater δ_{AB}. The data are indicative of the lower activation energy for inversion than those in the other systems.

Equations (1) to (3) were employed to calculate the exchange life-time τ at the intermediate temperature ranges which are listed in Tables 4 and 5. The Arrhenius activation energy E_a and the frequency factor A for the exchange process (Eq. (4)) were obtained from the best fitting line

TABLE 4. EXPERIMENTAL LINE-WIDTHS AND EXCHANGE LIFE-TIMES FOR I IN CHLOROFORM-d AND DIMETHYL-d_6 SULFOXIDE

Temp. °C	w for inner lines[a]		w for outer lines[a]		w for coalesced line[b]		τ msec
	h[c]	l	h	l	h	l	
			$CDCl_3$ ($w_0=1.20$ cps)				
0	1.45	1.45	1.80	—			714
10	1.80	1.70	—	—			325
50					—	6.00	8.42
60					5.30	3.50	3.74
70					3.15	2.30	1.78
			DMSO ($w_0=1.10$ cps)				
36					5.60	4.00	2.21
50					2.80	2.20	0.84
70					1.60	1.50	0.27_2
90					1.20	1.15	0.042_9
120					1.15	1.12	0.018_8

a) Data treated by Eq. (1).
b) Data treated by Eq. (3).
c) h and l stand for the AB-quartets at the higher and the lower applied magnetic field, respectively.

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15) From the ultraviolet spectral data, the dihedral angle between the two benzene rings is estimated to be about 45°[12] (H. Suzuki, This Bulletin, **32**, 1340, 1350, 1357 (1959); **33**, 109 (1960)).

TABLE 5. EXPERIMENTAL LINE-WIDTHS AND EXCHANGE LIFE-TIMES FOR II IN TETRACHLOROETHYLENE, CHLOROFORM-d AND DIMETHYL-d_6 SULFOXIDE

Temp. °C	*w* for inner lines		*w* for outer lines		*w* for coalesced line		τ msec
	h	l	h	l	h	l	
C_2Cl_4 (w_0=1.20 cps)							
0	1.60	1.60	1.80	2.30			467
10	1.80	1.85	—	3.30			247
60					4.05	3.10	3.69
70					2.60	2.15	1.80
80					2.00	1.60	0.91_5
90					1.60	1.40	0.45_8
100					1.50	1.30	0.27_6
$CDCl_3$ (w_0 = 1.20 cps)							
0	1.50	1.50	1.90	1.70			662
10	1.80	1.80	2.10	—			338
20	2.20	2.00	3.00	—			211
50					—	6.00	8.21
60					6.50	3.80	4.4_7
70					2.90	2.10	1.4_9
DMSO (w_0 = 1.05 cps)							
50					6.00	4.00	2.07
70					3.35	2.45	0.93
80					2.20	1.65	0.43_3
90					1.55	1.40	0.23_5
100					1.35	1.25	0.12_6
120					1.15	1.15	0.05_3

TABLE 6. ACTIVATION PARAMETERS FOR THE INVERSION OF I AND II IN SEVERAL SOLVENTS

	Solvent	E_a kcal/mol	log *A*
I	$CDCl_3$	16.9±1.0	13.6±0.8
	DMSO	15.6±1.2	13.6±0.9
II	C_2Cl_4	17.0±1.0	13.5±0.8
	$CDCl_3$	16.9±1.0	13.5±0.8
	DMSO	17.2±1.4	13.7±1.0

determined by the method of least squares.16) The results are summarized in Table 6. Although the number of solvents examined is quite limited, they cover wide varieties of the solvent properties; dielectric constant, polarity, basicity, viscosity,17) *etc.* From the data obtained for II in Table 6, it follows again that the kinetic parameters for inversion are, within the experimental error, almost independent of the solvents.18) Because the energy of activation for inversion of biphenyls such as II may be regarded to be governed by the non-bonded repulsion and the ring-strain in the activated state for the process, and because they are rather insensitive to the intermolecular interaction, the indifference to the change in solvent is not unreasonable.

To the contary, the activation parameters for the inversion of I in $CDCl_3$ and DMSO are decidedly different. Since DMSO is famous for its strong proton-accepting ability for phenols,19) the hydrogen bonding must be playing some role. Two mechanisms may then be considered to be operative. Firstly, the strong hydrogen bonding between the hydroxyl group of I and DMSO will

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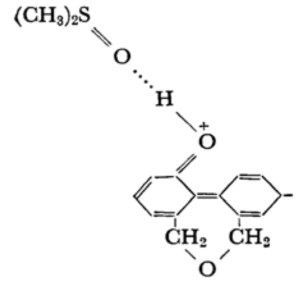
16) The probable errors in the values of E_a and log *A* thus determined are ±0.3 kcal/mol and ±0.2, respectively. For a more realistic estimate of the uncertainty in these kinetic paramaters, each point was marked as a rectangle corresponding to the uncertainty of the point; two straight lines with maximum and minimum slopes were drawn in such a manner as to pass through each rectangle. The probable errors thus obtained are listed in Table 6.

17) A change in viscosity of the medium will contribute to the width of the NMR lines investigated and may affect the activation parameters, but the contribution of this relaxation width is discarded from the constancy of the width of other lines in the same molecule, *e. g.*, that of CH_3O signal.

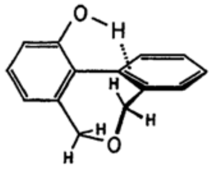
18) Graybill and Leffler11) examined the rates of racemization of dimethyl *o, o'*-dimethoxydiphenate in 23 solvents. The rates vary by about a factor of two and the activation energy has a range of 2.1 kcal/mol. There is a general tendency for the ester to racemize more rapidly in polar solvents and the alcoholic proton donor solvents ratard the racemization, although the latter solvents have not been tested for the present examples.

19) A. Wagner, H. J. Becjer and K.-G. Kottenhahn, *Chem. Ber.*, **89**, 1708 (1956); S. Ghersetti and A. Lusa, *Spectrochim. Acta,* **21**, 1067 (1965).

reduce the electronegativity of the hydroxyl oxygen and the consequent conjugation between the two benzene rings. This contribution III stabilizes the planar conformation corresponding to the activated state for inversion more than the nonplanar ground state. In effect E_a will be reduced relative to that of non-hydrogen bonded cases.



III



IV

Secondly, it has been shown by the infrared spectroscopy of the ν_{O-H} region that there is an intramolecular interaction between the hydroxyl group and the π-electrons on the benzene ring (IV) in the ground state of I in non-associative solvents, while no such intramolecular O–H$\cdots\pi$ interaction takes place in the planar 2-hydroxybiphenyl derivatives which may represent a model for the activated state for inversion.[12] The ground state of I in $CDCl_3$ is, therefore, stabilized with respect to the activated state by the energy of that interaction which is expected to be of the order of 1.5 kcal/mol.[20] Since DMSO is a powerful proton acceptor[19] and the hydroxyl group in I is essentially deprived of the intramolecular O–H$\cdots\pi$ interaction in this solvent, the ground state of I is not stabilized relative to the excited state. Accordingly E_a for inversion should be smaller in DMSO than in $CDCl_3$ by the amount of the energy of that O–H$\cdots\pi$ interaction (IV). The observed value is compatible with that obtained by the IR measurements.[12,20]

The experiments are now in progress to separate the contribution of the two factors.

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20) M. Ōki and H. Iwamura, This Bulletin, **34,** 1395 (1961).